

Internationally Harmonized Performance Standards (PS) for the Murine Local Lymph Node Assay (LLNA)

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ICCVAM, in conjunction with ECVAM and JaCVAM, developed internationally harmonized PS for the LLNA that can be used to evaluate modified versions of the LLNA. These PS include essential test method components, a minimum list of reference substances, and standards for accuracy and reliability. Essential test method components are structural, functional, and procedural elements of a validated test method that should be included in the protocol of a mechanistically and functionally similar proposed test. Essential components of the LLNA include topical application of the test substance to the mouse ears, measurement of lymphocyte proliferation in lymph nodes draining the application site, and use of the maximum soluble dose that does not result in systemic toxicity or excessive local irritation. The list of reference substances includes 13 sensitizers and 5 nonsensitizers. Four optional substances are included to demonstrate superior performance relative to the LLNA. The accuracy and reliability standards are based on the performance of the LLNA as compared to human and guinea pig results. An update to OECD TG 429 has been proposed to include these PS, which will facilitate more rapid and efficient validation/acceptance of modified LLNA protocols. New improved versions of the LLNA that offer other advantages are expected to result in broader use of the LLNA, which will further reduce and refine animal use for allergic contact dermatitis assessments. ILS staff supported by NIEHS contract N01-ES-35504. This abstract reflects the views of the authors and has not been approved by the US CPSC or other agencies.